

We claim:

1. A polymer synthesizing apparatus comprising
  - a. a base on which sits a synthesis case, a synthesis block, a means of moving the synthesis block and the lower ends of supports for a reagent shelf;
  - 5        b. the synthesis case comprising a load station, drain station, an aqueous reagent filling station, and a non-aqueous reagent filling station; the synthesis case having a cover, a first and a second side, a first and a second end, and a bottom side which contacts the base;
  - c. the bottom side of the synthesis case having a top face in which there are
  - 10        tracks for the synthesis block;
  - d. the synthesis block being capable of moving back and forth on the tracks in the synthesis case, the synthesis block having a top face and an opening in the top face for a multiwell plate, the synthesis block also having a collection area under the multiwell plate to drain spent reagents and to optionally accommodate a sample tray;
  - 15        e. a means of moving the synthesis block back and forth on the tracks in the synthesis case;
  - f. the load station comprising a sealable opening in the synthesis case through which a multiwell plate can be inserted into the synthesis block;
  - g. a reagent shelf connected to the upper ends of the supports, which is
  - 20        capable of supporting a plurality of reagent containers, each reagent container having a tube connecting to a gas source, the gas source having the effect of expelling a controlled amount of reagent from the container, and a tube for dispensing the reagent, the dispensing tube connecting at its other end to valves that have additional tubes connected to multi-channel manifolds, which in turn have tubes connecting to nozzle blocks at the
  - 25        aqueous and non-aqueous filling stations;
  - h. the valves being actuated by the computer to dispense fluid to desired wells in the multiwell plate; and
  - i. a means of draining liquid from the synthesis plate.
- 30        2. The polymer synthesizer of claim 1 wherein the means of moving the synthesis block comprise a pulley, cable and motor.

3. The polymer synthesizer of claim 1 wherein the means of draining the liquid from the synthesis plate comprises a means for applying a positive pressure above the synthesis plate to force liquid to drain.

5 4. The polymer synthesizer of claim 1 wherein the means for draining the liquid from the synthesis plate comprises:

- a pressurized gas source,
- a pressurized gas inlet on the synthesis case,
- a pressure plate,
- 10 a support block,
- a diaphragm which forms a seal between the top plate and one side of the pressure plate and the support block,
- a motive means connected to the pressure plate and capable of moving the pressure plate up,
- 15 and at least one sealing gasket to contact and form a seal with the synthesis plate, whereby gas enters through the pressurized gas inlet and presses down the diaphragm, which in turn lowers the pressure plate and gasket to form a seal over the synthesis block and increases pressure above the wells, which expels the liquid contents of the wells.

20 5. The draining means of claim 4, wherein the motive means is a set of springs.

6. An automated method of draining synthesis wells in a polymer synthesizer, the method comprising

- 25 a. providing a drain station apparatus, comprising a pressurized gas inlet on a synthesis case, a pressure plate, a support block, a diaphragm which forms a seal between the top plate and one side of the pressure plate and the support block, a motive means connected to the pressure plate and capable of moving the pressure plate up after it is pushed down by air pressure, and a plurality of sealing gaskets,
- 30 b. supplying pressurized gas at the pressurized gas inlet,
- c. increasing a distensible space between the pressure plate and diaphragm,

d. pressing down the diaphragm for contact with the pressure plate with at least one gasket connected to it,

e. the pressure plate and gasket(s) pressing down onto a multiwell plate,

f. creating a seal with the multiwell plate

5 g. compressing the gasket and the space at each well's inlet, and

h. expelling liquid or reagents present in the well from the well outlets.

*Rak 126* ~~7/8~~ 8. The polymer synthesizer of claim 1 wherein the tracks in the synthesis case are Teflon coated.

~~9~~ 9. An automated method for synthesizing polymers, specifically oligonucleotides comprising:

a. providing the polymer synthesizer of claim 1 with appropriate reagents;

b. obtaining a multiwell plate;

15 c. placing controlled pore glass beads coated with dimethoxytrityl (DMT) protecting group into each well;

d. placing the multiwell plate in the synthesizer block and securing the multiwell plate therein;

e. moving the synthesizer block to the water tolerant filling station;

20 f. adding trichloroacetic acid (TCA) to any or all 8 wells at a time and briefly incubating the mixture;

g. moving the synthesis block to the drain station and pressurizing the wells to expel the spent reagent;

h. repeating steps e-g at least once;

25 i. moving the synthesizer block to the water tolerant filling station,

j. adding acetonitrile (ACN) to 8 wells at a time and briefly incubating the mixture;

k. moving the synthesis block to the drain station and pressurizing the wells to expel the spent reagent;

30 l. repeating steps i-k at least once;

m. moving the synthesizer block to the water-sensitive filling station;

n. adding tetrazole in acetonitrile and an appropriate base to each well and incubating;

o. moving the synthesis block to the drain station and pressurizing the wells to expel the spent reagent;

5 p. moving the synthesis block to the water tolerant filling station;

q. adding a solution of Cap A and Cap B and incubating;

r. moving the synthesis block to the drain station and pressurizing the wells to expel the spent reagent;

s. repeating steps p-r at least once;

10 t. moving the synthesis block to the water-tolerant filling station and adding I<sub>2</sub> oxidizing reagent, incubating, and pressure filtering;

u. dispensing ACN into the well, pressure filtering, and repeating ACN addition and pressure filtering at least once;

15 v. repeating steps e-u to add bases until the desired oligonucleotides are synthesized; and

w. adding an appropriate reagent to separate the oligonucleotides from the CPG beads, incubating the reaction mixture, and pressure filtering the wells into wells of a sample tray or second multiwell plate placed in the opening lower in the synthesis block.

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